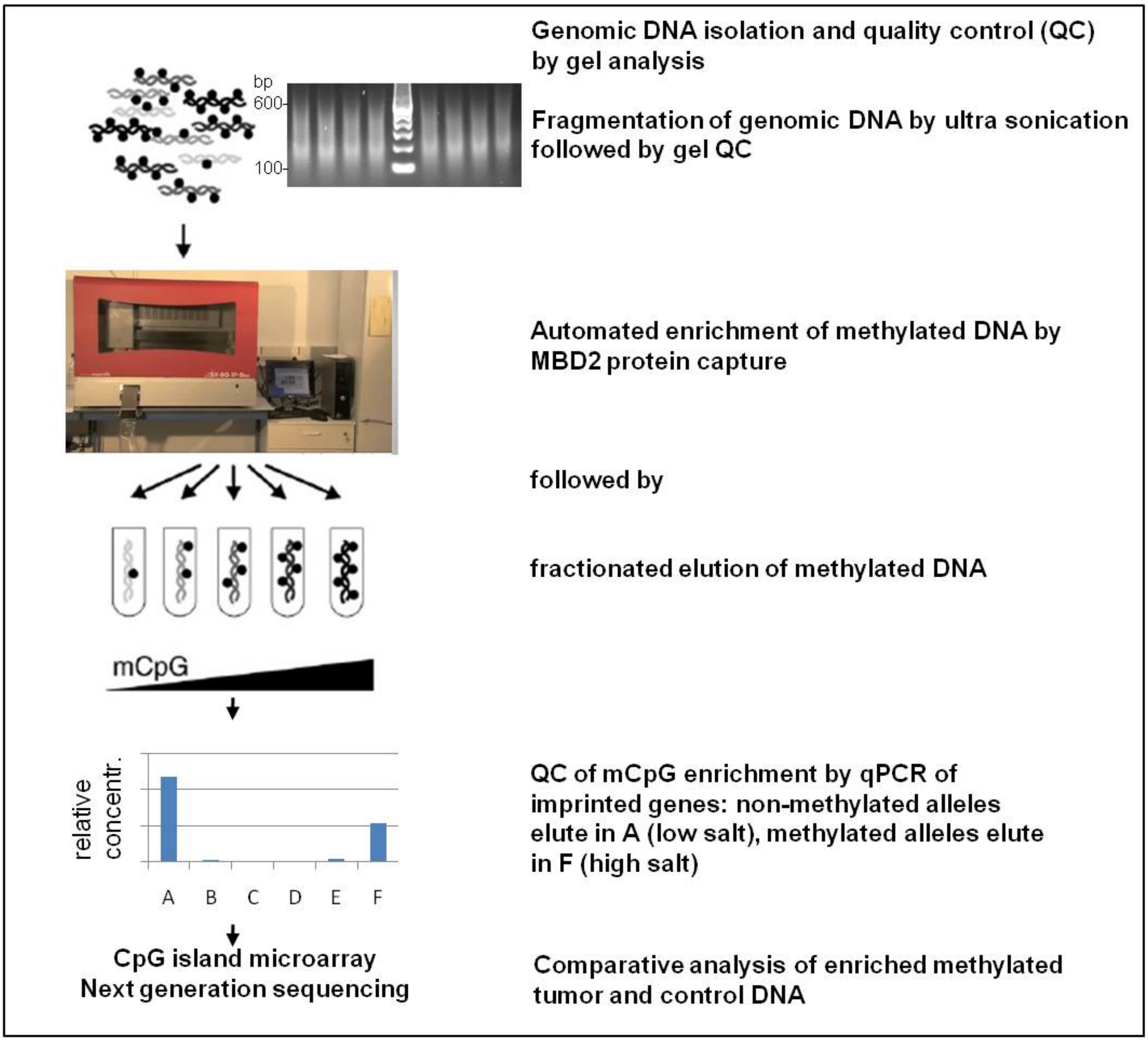
Genome-wide methylation (Methylome) analysis

A common hallmark in tumorigenesis is the silencing of tumor suppressor genes by promoter hypermethylation. We apply automated **methyl-CpG immunoprecipitation** (**MCIp**; Gebhard et al. 2006) to enrich for hypermethylated tumor DNA sequences. Using a recombinant methyl-CpG-binding domain protein, MBD2, for initial DNA capture, weakly methylated DNA is then released at low, highly methylated DNA at high salt concentrations. Enriched methylated DNA of tumor and control tissue samples is analysed by dual-color CpG island microarray hybridization or by next generation sequencing. Differentially methylated regions (DMRs) are validated by MassARRAY mass spectrometry.



Genomic DNA isolation and quality control (QC) by gel analysis

Fragmentation of genomic DNA by ultra sonication followed by gel QC

Automated enrichment of methylated DNA by MBD2 protein capture

followed by

fractionated elution of methylated DNA

QC of mCpG enrichment by qPCR of imprinted genes: non-methylated alleles elute in A (low salt), methylated alleles elute in F (high salt)

Comparative analysis of enriched methylated tumor and control DNA

Gebhard C, Schwarzfischer L, Pham TH, et al. Genome-wide profiling of CpG methylation identifies novel targets of aberrant hypermethylation in myeloid leukemia. Cancer Res 2006; 66(12):6118-28